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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ZHENG, LI	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,720	ALLISON, RICHARD F.	
	Examiner	Art Unit	
	LI ZHENG	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *236 and 238-306* is/are pending in the application.

4a) Of the above claim(s) *242,259 and 275-306* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *236,238-241,243-258 and 260-274* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/3/2009;4/10/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 236 and 238-306 are pending.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 3, 2009 has been entered.

Applicant's cancellation of claim 237 and amendments to claims 236, 241, 243, 249-256, 264-266 and 270 filed on March 3, 2009 are acknowledged.

Claims 242, 259 and 275-306 are withdrawn for being drawn to non-elected inventions.

Claims 236, 238-241, 243-258 and 260-274 are examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The rejections and objections that are not recited in this Office Action are considered as being withdrawn.

Claim Objections

5. Claim 236 is objected to for missing the recitation “and" after part ii) and before part iii).

Claim Rejections - 35 USC § 112

6. Claims 236, 238-241, 243-258, 262-263, 266-267 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 236, the last step of the method in instant claims is inconsistent with the preamble. The last step only results in synthesis of an RNA complementary to an RNA transcript of the recombinant DNA in a transgenic plant, whereas the preamble states that the method is for producing a heterologous polypeptide.

Claims 239 and 262 recite the limitation "the eukaryotic constitutive promoter" in line 2. There is insufficient antecedent basis for this limitation in the claim.

In claims 240 and 263, the recitation “a heterologous polypeptide “ in line 2 renders the claim indefinite. It is unclear “a heterologous polypeptide “ refers to the heterologous polypeptide in claim 236 or not. The metes and bounds are not clear.

In claims 243 and 266, the recitation “the 3’ UTR of a first positive strand single-stranded RNA plant virus is a 3’ UTR of a first positive strand single-stranded RNA plant virus having no DNA stage” renders the claim indefinite. It is unclear what " a first positive strand single-stranded RNA plant virus” refers to. The metes and bound are not clear. It is suggested to recite further limitation as –wherein the first positive strand single-stranded RNA is a positive strand single-stranded RNA with no DNA stage--.

Claim 245 recites the limitation "said DNA molecule" in line 2. There is insufficient antecedent basis for this limitation in the claim.

In claim 253, the recitation “the cDNA of a second positive strand single-stranded RNA plant virus” renders the claim indefinite. It is unclear what " a second positive strand single-stranded RNA plant virus” refers to. The metes and bounds are not clear.

In claim 254, the recitation “the cDNA of a second positive strand single-stranded RNA plant virus is a cDNA of a second positive strand single-stranded RNA plant virus having no DNA stage” renders the claim indefinite. It is unclear what " a second positive strand single-stranded RNA plant virus” refers to. The metes and bound are not clear. It is suggested to recite further limitation as –wherein the second positive strand single-stranded RNA is a positive strand single-stranded RNA with no DNA stage--.

Claim 257 recites the limitation "the RNA comprising at least one sequence encoding a polypeptide component of an RNA virus replication complex" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

Claim 258 recites the limitation "the molar concentration ratio of heterologous polypeptide in a cell" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

In claim 267, the recitation “the 3’UTR of a positive strand single-stranded RNA plant virus” renders the claim indefinite. It is unclear what " a positive strand single-stranded RNA plant virus” refers to. The metes and bounds are not clear.

Claim Rejections - 35 USC § 112

Written Description

7. Claim 236, 238-241, 243-258 and 260-274 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a method of producing a heterologous polypeptide in any transgenic plant cell comprising a) providing a transgenic plant cell comprising a DNA molecule containing a promoter operably linked to a DNA sequence containing a sequence complementary to a coding sequence for a heterologous polypeptide, a sequence complementary to any IRES and a 3’ UTR of a first positive strand single-stranded RNA virus; b) growing the transgenic cells; and c) provide stimulus for synthesis of an RNA complementary to an RNA transcript of the

recombinant DNA, the DNA molecule used in the method and the transgenic cells produced by the method.

The specification prophetically teaches a method for producing a heterologous polypeptide in any transgenic cell (paragraphs [0082]-[0084]). The specification describes various promoters (paragraph [0047]), the heterologous genes (paragraph [0048]), the IRES elements (paragraphs [0049]-[0053]), 3'UTR regions (paragraphs [0054]-[0060]) and viruses that can be used as stimulus (paragraphs [0061]-[0063]). The specification also teaches that the replication complex of BMV could recognize and synthesize a complementary copy of a CCMV transgene that contains a complete 3' UTR (paragraph [0080]).

The specification fails to describe a genus of any 3' UTR of any positive single-stranded RNA that can be stimulated by any means. The specification fails to describe the conserved structure for those 3' UTRs and their corresponding stimuli that can be used in instant invention. The specification only teaches that the replication complex of BMV could recognize and synthesize a complementary copy of a CCMV transgene that contains a complete 3' UTR (paragraph [0080]). In other word, the specification only describe 3' UTR of CCMV can be stimulated by infection of BMV to synthesize an RNA complementary to the RNA transcript of the DNA sequence.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise

definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of 3'UTR that can be stimulated by any stimulus. Applicants only describe a single species, 3' UTR of CCMV. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for 3'UTR that that can be stimulated by a stimulus, it remains unclear what features such a 3'UTR. Since said genus has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Scope of Enablement

8. Claims 236, 238-241, 243-258 and 260-274 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a heterologous polypeptide in plant comprising a) providing a transgenic plant comprising a DNA molecule containing a plant promoter operably linked to a DNA sequence containing a sequence complementary to a coding sequence for a heterologous polypeptide, a sequence complementary to an IRES from a plant virus and a 3' UTR of CCMV; b) growing the transgenic plant ; and c) stimulating synthesis of an RNA complementary to the RNA transcript of the DNA sequence by infecting the transgenic plant with BMV, does not reasonably provide enablement for a method for producing heterologous polypeptide by using any promoter, any 3' UTR from any positive single stranded RNA virus or by providing any stimulus for synthesis of an RNA complementary to any RNA transcript of the recombinant DNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the

invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The instant claims are drawn to a method of producing a heterologous polypeptide in any transgenic plant cell comprising a) providing a transgenic plant cell comprising a DNA molecule containing a promoter operably linked to a DNA sequence containing a sequence complementary to a coding sequence for a heterologous polypeptide, a sequence complementary to any IRES and a 3' UTR of a first positive strand single-stranded RNA virus; b) growing the transgenic cells; and c) provide stimulus for synthesis of an RNA complementary to an RNA transcript of the recombinant DNA, the DNA molecule used in the method and the transgenic cells produced by the method.

The specification prophetically teaches a method for producing a heterologous polypeptide in any transgenic cell (paragraphs [0082]-[0084]). The specification describes various promoters (paragraph [0047]), the heterologous genes (paragraph [0048]), the IRES elements (paragraphs [0049]-[0053]), 3'UTR regions (paragraphs [0054]-[0060]) and viruses that can be used as stimulus (paragraphs [0061]-[0063]). The specification also teaches that the replication complex of BMV could recognize and synthesize a complementary copy of a CCMV transgene that contains a complete 3' UTR (paragraph [0080])

The specification fails to reduce the invention to practice. The only working example is only to demonstrate that the replication complex of BMV could recognize and synthesize a complementary copy of a CCMV transgene that contains a complete

3' UTR. The working example does not use IRES to drive the translation of the heterologous gene. The claims, however, are broadly drawn to a method for producing heterologous polypeptides in plant cell using any promoter and any 3'UTR from any positive single-stranded RNA or any stimulus for synthesis of an RNA complementary to any RNA transcript of the recombinant DNA.

First, clearly, only plant promoter is enabled for instant invention since the method is practice in plant cells.

Second, the RNA transcript of the recombinant DNA needs to encompass all the nucleotide sequence encoded by all three parts of the DNA sequence in claim 236. Any transcript lacking any part of the DNA sequence would not be enabled since coding region, IRES and 3'UTR are all required.

Third, as discussed in the written description rejection, the specification fails to provide guidance on how to obtain 3' UTR from any unexemplified positive single-stranded virus that can be stimulated by any unexemplified means to synthesize the RNA complementary to the RNA transcription of the DNA sequence. There is no assay provided by the specification to perform the selection of 3'UTR since the means of stimulation is unspecified. Undue experimentation would be required for a person skilled in the art to identify both 3' UTR and its corresponding stimulus.

Therefore, given the claim breadth, lack of further guidance and additional working example, unpredictability of the art, undue experimentation would have been required for a person skilled in the art to practice the invention.

Summary

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Li Zheng/

Examiner, Art Unit 1638